mice had significantly poorer cGVHD scores than control mice (WT BM cells into WT recipients), suggesting the role of host parenchymal tissue cell expression of B7H1 in cGVHD. Taken together, the PD-1 axis, especially B7H1 expression on recipients, regulates the frequency of IL-17+ IFNg+ T cells and contributes to the pathogenesis of cGVHD.

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Post-Transplant Cyclophosphamide (PTC) As Sole Graft Versus Host Disease (GVHD) Prophylaxis in Patients Undergoing HLA Matched Sibling Donor Stem Cell Transplant (SCT) for Severe Aplastic Anemia (SAA)

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Between September 2010 and June 2012, 15 patients with SAA underwent HLA identical sibling donor SCT using Fludarabine 180 mg/m2 IV over 6 days and Cyclophosphamide 100 mg/kg IV over 2 days. Five patients had in addition a single fraction of Total Body irradiation (TBI) 200 cGy. Cyclophosphamide 50 mg/kg/day IV on day +3 and +4 was the sole GVHD prophylaxis. G-CSF mobilized peripheral blood stem cells (PBSC) was the graft source. Ten males and 5 females with a median age of 25 years (range: 8 – 42) had SCT. Median PBSC cell dose infused was 9.5 x 106 CD34/Kg (range: 5.4 – 17.2). Thirteen engrafted (86.6%) with median neutrophil and platelet engraftment of 15.4 days (range: 15-17) and 16.6 days (range: 12-32) respectively. Grade II–IV GVHD seen in 3 patients (23%) at 42, 49 and 68 days post SCT. Two responded to combination of cyclosporine and prednisolone while one patient with grade IV GVHD expired 64 days post SCT. Of 11 evaluable patients, 4 (36.3%) developed chronic GVHD which was limited in all. Two patients with de novo chronic GVHD were managed with prednisolone alone. Overall 7 patients (46.6%) have not required any immunosuppression after SCT while 3 have required immunosuppressive therapy for 114, 127 and 225 days respectively At a median follow up of 11 months (range: 1 – 22), 11 (73.3%) are alive and well including 7 patients who did not require any immunosuppressive therapy following SCT. The use of post transplant cyclophosphamide as GVHD prophylaxis following sibling donor transplant for SAA is associated with low rates of GVHD. A large number (46%) did not require any immunosuppression post SCT. Larger studies are required to understand the utility of this prophylaxis in sibling donor transplants for aplastic anemia.

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Efficacy and Safety of Immunomodulation with Fast Withdrawal of Immunosuppression (FWI) and Donor Lymphocyte Infusions (DLI) for Prevention of Relapse in Children Receiving Allogeneic Hematopoietic Stem Cell Transplant (HCT) for Hematologic Malignancies

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Persistence of mixed chimerism (MC) following myeloablative HCT in pediatric hematologic malignancies is related to a high risk of relapse. We initiated a prospective study of FWI and DLI in patients with MC at 30 days post-transplant. We are reporting preliminary results on 43 enrolled patients with a mean age of 10±6.5(SD) years. Fifty-eight percent of patients had myeloid malignancies, 40% lymphoid malignancies and 2% had biphenotypic leukemia. Based on day +30 bone marrow and peripheral blood chimerism results, 26/43 (60%) patients were found to have MC, and were assigned to the intervention arm of the study consisting of FWI and DLI; 12 patients (28%) had full donor chimerism (FDC) or early graft-versus host disease (GVHD) and were assigned to observation arm, and 5 (12%) could not be assigned to either arm due to early death or relapse. FWI started at a median of day +50 (range 40-85), and ended at a median of day +75.5 (range 49-113). Following FWI, 9 patients (35%) converted to FDC. Of 17 patients who remained MC following FWI, 15 proceeded to DLI, 1 did not receive further intervention due to GVHD and one relapsed prior to DLI. Acute GVHD developed in 3/26 (12%) patients undergoing FWI and in 9/12 (75%) of patients in the observation arm ($P < .01$). Two patients undergoing intervention developed grade II aGVHD which resolved and 1 developed grade IV aGVHD that progressed to fatal cGVHD of the lungs. In the observation arm, 2 patients developed grade I, 5 developed grade II, 2 developed grade III, and 1 developed grade IV aGVHD. Chronic GVHD developed in 6 patients (2 in the intervention and 4 in the observation arm). One of 6 patients developed de novo cGVHD, following DLI. The incidence of acute and/or chronic GVHD was 15% in the intervention arm of the study. Toxic death rate due to GVHD was 4%. There were 11 events (3 treatment-related deaths and 8 relapses). Mean follow-up of living patients was 17.6±10 (SD) months. EFS for the entire cohort was 71±7(SD)% and was not significantly different between the observation arm and the intervention arm. Ten patients (23%) had evidence of disease by flow or cytogenetics, at the time of HCT. Based on chimerism results, 4 were assigned to the intervention arm, 3 to the observation arm, and 3 could not be assigned to any arm of the study due to early relapse or death. EFS was significantly lower in patients with positive disease prior to transplant than in those without evidence of disease (EFS 27±15% vs. 86±7%). Among 26 patients undergoing intervention, relapse was significantly more common ($P = .014$) in patients with positive disease pre-transplant. Our data indicate that post-transplant immunomodulation is safe and has overall low GVHD risk (15%). Our schedule of FWI was not adequate to prevent relapse in patients coming to transplant with persistent disease. We would recommend an earlier, (day 30) and more aggressive schedule of immunosuppression withdrawal for these patients.

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From Murine Model to Clinical Trial of Graft-Versus-GVHD, a Second Transplantation From Another Donor for the Rescue From Refractory Acute GVHD

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Background: GVHD is still a major obstacle in allogeneic transplantation despite the progress of immunosuppressive drugs and cell therapy such as mesenchymal stem cells. GVHD is caused by donor lymphocytes, mainly T cells,